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Applicant/Proprietor: MEDVET SCIENCE PTY. LTD.

Decision on the request for further processing under Rule 135(3) EPC

The request for further processing received on 12.09.08 has been granted (Art. 121(2) EPC).

☑ The legal consequence notified in the communication dated 04.07.08 that the application was deemed to be withdrawn shall not ensue.

☐ The refusal of the application dated ..... shall not ensue.

☐ The legal consequence notified in the communication dated ..... that the particular loss of rights occurred shall not
- ☐ ensue.
- ☐ ensue for the following contracting state(s):

☐ The time limit set in the communication dated ..... is deemed to have been met.

The procedure shall be continued/the particular loss of rights shall not ensue (Art. 121(3) EPC).

For the Examining Division

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RFPR4=3

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A method of modulating sphingosine kinase functional activity *in vitro*, said method comprising contacting said sphingosine kinase with an effective amount of an agent for a time and under conditions sufficient to modulate phosphorylation of said sphingosine kinase wherein said agent agonises or antagonises the interaction between sphingosine kinase and a phosphorylation catalyst or acts as a phosphorylation catalyst of sphingosine kinase.

2. A method of modulating cellular activity *in vitro*, said method comprising contacting said cell with an effective amount of an agent for a time and under conditions sufficient to modulate the phosphorylation of sphingosine kinase wherein said agent agonises or antagonises the interaction between sphingosine kinase and a phosphorylation catalyst or acts as a phosphorylation catalyst of sphingosine kinase.

3. The method according to claim 1 or 2 wherein said sphingosine kinase is human sphingosine kinase.

4. The method according to any one of claims 1-3 wherein said phosphorylation is modulated at S^{225}.

5. The method according to claim 4 wherein said agent binds, links or otherwise associates with S^{225}.

6. The method according to any one of claims 1-5 wherein modulation of said phosphorylation is modulation of proline-directed protein kinase catalysed phosphorylation.

7. The method according to claim 6 wherein said proline directed kinase is ERK1, ERK2 or CDK2.

8. The method according to claim 7 wherein said proline directed kinase is ERK2.

9. The method according to any one of claims 1-8 wherein said modulation is down-regulation.

10. An agent which antagonises the interaction between sphingosine kinase and a phosphorylation catalyst for use in therapeutically downregulating inflammation or cellular proliferation.

11. An agent which agonises the interaction between sphingosine kinase and a phosphorylation catalyst or which acts as a phosphorylation catalyst for use in therapeutically stimulating cellular proliferation or inflammation.

12. The agent according to claim 10, wherein said agent is for use in the treatment of a condition which is characterised by inflammation or unwanted cellular proliferation in a mammal.

13. The agent according to any one of claims 10 to 12 wherein said sphingosine kinase is human sphingosine kinase.

14. The agent according to any one of claims 10-13 wherein said phosphorylation is modulated at S^{225}.

15. The agent according to claim 14 wherein said agent binds, links or otherwise associates with S^{225}.

16. The agent according to any one of claims 10-15 wherein said phosphorylation catalyst is a proline-directed protein kinase.

17. The agent according to claim 16 wherein said proline directed protein kinase is ERK1, ERK2 or CDK2.

18. The agent according to claim 17 wherein said proline directed kinase is ERK2.

19. The agent according to claims 10-11 or 12-18 wherein said inflammation is induced by TNF.

20. The agent according to claim 10 or 12-18 wherein said cellular proliferation is neoplastic proliferation, TNF-induced cellular proliferation and/or anti-apoptotic activity.

21. The agent according to claim 10 or 12-18 wherein said inflammation is inflammatory mediator production and/or adhesion molecule expression.

22. The agent according to claim 10 or 12-18 wherein said inflammation is associated with rheumatoid arthritis, atherosclerosis, asthma, autoimmune disease or inflammatory bowel disease.

23. Use of an agent in the manufacture of a medicament for the treatment of a condition in a mammal, which condition is characterised by inflammation or unwanted cellular proliferation, wherein said agent antagonises the interaction between sphingosine kinase and a phosphorylation catalyst.

24. Use according to claim 23 wherein said sphingosine kinase is human sphingosine kinase.

25. Use according to any one of claims 23-24 wherein said phosphorylation is modulated at S^{225}.

26. Use according to claim 25 wherein said agent binds, links or otherwise associates with S^{225}.

27. Use according to any one of claims 23-26 wherein said phosphorylation catalyst is

a proline-directed protein kinase.

28. Use according to claim 27 wherein said proline directed kinase is ERK1, ERK2 or CDK2.

29. Use according to claim 28 wherein said proline directed kinase is ERK2.

30. Use according to claim 23-29 wherein said inflammation is induced by TNF.

31. Use according to claim 23-29 wherein said condition is a neoplastic condition.

32. Use according to claim 23-30 wherein said inflammation is inflammatory mediator production and/or adhesion molecular expression.

33. Use according to claim 23-30 or 32 wherein said inflammatory condition is rheumatoid arthritis, atherosclerosis, asthma, autoimmune disease or inflammatory bowel disease.

34. An isolated sphingosine kinase variant comprising a mutation at one or more of S^{148}, S^{181}, Y^{184}, S^{225} or T^{250}, wherein said variant exhibits ablated or reduced phosphorylation capacity relative to wild-type sphingosine kinase or a functional derivative, homologue or analogue thereof.

35. An isolated sphingosine kinase variant comprising a mutation at one or more of S^{148}, S^{181}, Y^{184}, S^{225} or T^{250}, wherein said variant exhibits enhanced or up-regulated phosphorylation capacity relative to wild-type sphingosine kinase or a functional derivative, homologue or analogue thereof.

36. The isolated variant of claim 34 wherein said variant comprises an amino acid sequence with a single or multiple amino acid substitution and/or deletion of amino acid S^{225}.

37. The isolated variant of claim 36 wherein said substitution is a Ser^{225} Ala substitution.